Reproducibility of Activation Patterns: Measurement of Group and Subject Effects During Motor Learning

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Introduction. We studied activation pattern reproducibility for a figure tracing task using [^{15}O]water PET and linear discriminant analysis. Reproducible canonical eigenimages (CEs)—from a Canonical Variates Analysis (CVA) of PCA eigenvectors from Scaled Subprofile Model (SSM) preprocessing—were identified using twofold cross-validation resampling [1]. Pattern reproducibility histograms were used to test for: (1) reproducible multidimensional subspaces and (2) the influence of individual subjects on pattern reproducibility.

Methods. 18 right-handed controls were scanned while tracing a path along the perimeter of a five-pointed star. Each scanning session consisted of 1 baseline trial (no tracing), 8 tracing trials and a final baseline. The number of stars traced and tracing errors were recorded for each trial. CE reproducibility was assessed for an SSM/CVA classification of 10 groups (10 scans/subject) reflecting the possible nine-dimensional, within-subject temporal structure of the 18 controls across repeated baseline and tracing trials. For each of the 9 CEs the two CE patterns from each of 250 randomly chosen pairs of independent groups (9 subjects/group) were correlated and used to form reproducibility histograms (Fig. 1). For CE 2 the least and most reproducible patterns from each of the 250 pairs of CEs were identified by correlating each pattern with the average CE of the pair having the highest correlation. Subject influence was ranked by recording the number of times/250 pairs that each subject was included in the group producing the most reproducible pattern. This result was compared with the null hypothesis that subjects randomly contribute to groups with the most reproducible pattern, i.e., a binomial distribution, p=0.5 and N=250. The tracing task performance of identified subgroups was then compared (Fig. 2).

Fig. 1: Reproducibility Histograms of 9 CEs.

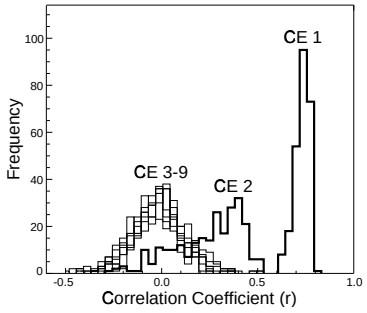
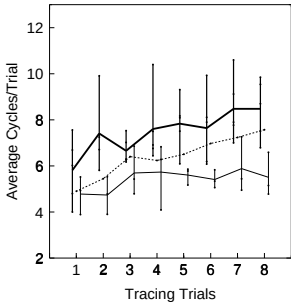


Fig. 2: Performance of CE2 Subject Subgroups.



Results. In **Fig. 1** the histograms for CE 3-9 are centered on zero indicating no significant reproducibility, while the CE1 and much of the CE2 histogram are significantly different from zero. CE1 canonical variates demonstrate that the CE1 histogram reflects the reproducibility of the basic two-state, baseline-tracing motor response, which is uniform across tracing trials. CE1 contains the expected motor system activations [2]. CE2 canonical variates reflect a linear trend with time across the 10 scans/subject, including the final baseline scan. The CE2 activation pattern is discussed in [2]. For CE2, ranking subject influence for the 9-subject groups with the most reproducible patterns identified (1) 3/18 subjects that occurred more frequently than expected (**Fig. 2:** thin solid lines, lower mean & range plots), (2) 10/18 subjects that occurred randomly (**Fig. 2:** dotted line, middle mean plot) and (3) 5/18 subjects that occurred less frequently than expected (**Fig. 2:** thick solid lines, upper mean & range plots)—all tests, $p < 0.05$, uncorrected. Over the course of learning during the eight tracing trials the 5/18 group's performance was characterized by higher speed/lower accuracy compared with the lower speed/higher accuracy of the 3/18 group.

Conclusions. The linear time trend of the reproducible CE2 pattern is associated with changes in skilled performance and may reflect motor learning processes which are not shared by the 5/18 subject group. We have demonstrated that an exploratory analysis based on reproducibility histograms may be used to identify (1) reproducible multidimensional activation subspaces and (2) subgroups of subjects with significant task performance and activation pattern differences without prior hypotheses or knowledge that such subgroups exist.

References.

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2. Frutiger S, et al. Submitted to 5th Int. Conf. On Functional Mapping of the Human Brain, Dusseldorf, 1999